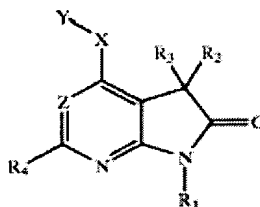


**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A compound of Formula 1



or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof, wherein:

R<sub>1</sub> is H or methyl;

each of R<sub>2</sub> and R<sub>3</sub> is independently H, halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, or (C<sub>1</sub>-C<sub>3</sub>)alkoxy; or R<sub>2</sub> and R<sub>3</sub> taken together form an optionally substituted methyldiene or a 3- to 7-membered ring optionally comprising 0-3 heteroatoms;

R<sub>4</sub> is H, methyl, trifluoromethyl, (C<sub>1</sub>-C<sub>4</sub>)alkyl, alkoxy, amido, amino, or optionally substituted aryl;

X is a chemical bond, ethynyl, -O-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -NR<sub>5</sub>C(O)-, or -NR<sub>5</sub>-, wherein R<sub>5</sub> is H, methyl, or substituted methylene;

Y is a 5- to 10-membered mono or bicyclic, saturated, unsaturated, or aromatic ring comprising 0-3 heteroatoms and optionally substituted; and

Z is N or CR<sub>6</sub>, wherein R<sub>6</sub> is H, halogen, nitro, cyano, alkoxyl, sulfonamide, amino, or amide.

2. (Original) The compound of claim 1 wherein X is a chemical bond, -O-, -S-, or -NR<sub>5</sub>-.

3. (Original) The compound of claim 1 wherein Y is selected from the group consisting of phenyl, indolyl, indolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-

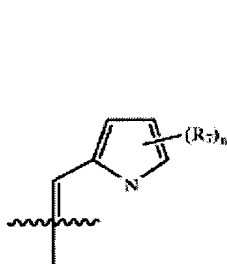
benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl, benzotriazolyl, pyridyl, pyrimidyl, 4-substituted piperazin-1-yl, morpholino, piperidinyl, pyrrolidin-1-yl, furanyl, thiophenyl, pyrrolyl, pyrazolyl, imidazolyl, pyridopyrrolyl, pyridazopyrrolyl, pyrimidopyrrolyl, pyrazopyrrolyl, pyridofuranyl, and derivatives thereof.

4. (Cancelled)

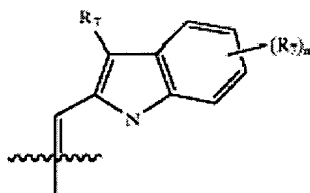
5. (Original) The compound of claim 1 wherein  $R_2$  and  $R_3$  are both H, halogen, or methyl.

6. (Original) The compound of claim 1 wherein  $R_2$  and  $R_3$  are taken together to form a ring selected from the group consisting of 1,3-dioxolane, 1,3-dioxane, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

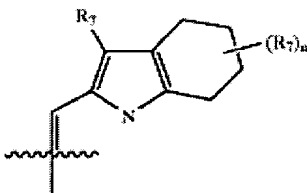
7. (Original) The compound of claim 1 wherein  $R_2$  and  $R_3$  are taken together to form an optionally substituted methyindene selected from those of Formulas 1a-1n:



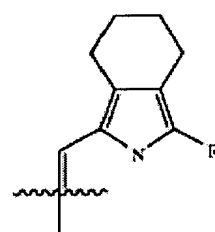
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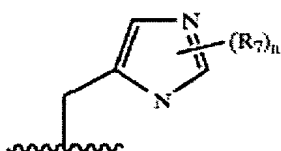
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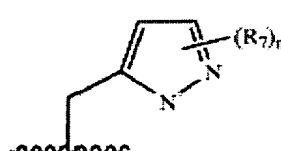
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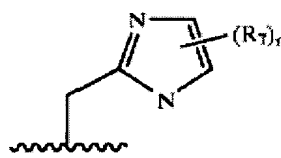
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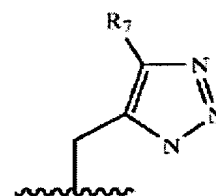
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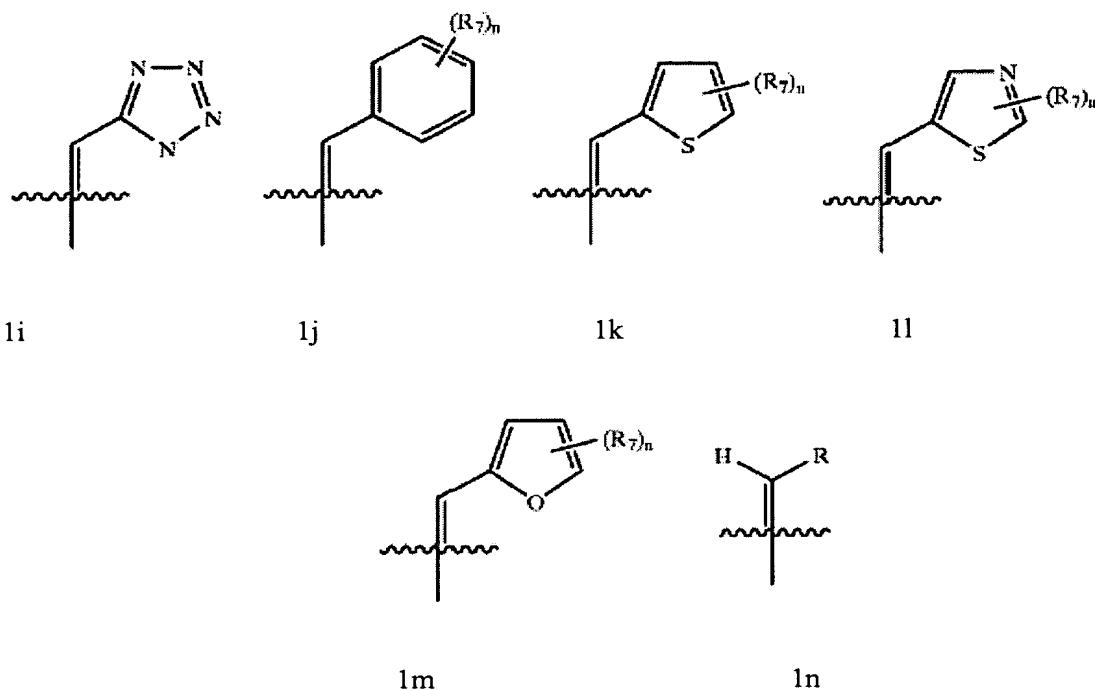
1f



1g



1h



wherein:

$n$  is an integer of 0-3;

each  $R_7$  is independently H, alkyl, carboxylic acid, amine, halogen, nitro, cyano,  $X_1$ ,  $X_2$ -(C-C<sub>4</sub>)alkyl- $R_8$ ,  $X_2$ -(C<sub>1</sub>-C<sub>4</sub>)alkenyl- $R_8$ , or  $X_2$ -(C<sub>1</sub>-C<sub>4</sub>)alkynyl- $R_8$ ;

$X_1$  is -C(O)NR<sub>9</sub>-, -NR<sub>9</sub>C(O)-, -C(O)O-, C(O)R<sub>11</sub>, -OC(O)-, -O-, -NR<sub>9</sub>-, -S-, -S(O<sub>2</sub>), or -S(O<sub>2</sub>)NR<sub>9</sub>-;

$X_2$  is a chemical bond, -C(O)NR<sub>9</sub>-, -NR<sub>9</sub>C(O)-, -C(O)O-, C(O)R<sub>11</sub>, -OC(O)-, -O-, -NR<sub>9</sub>-, -S-, -S(O<sub>2</sub>), or -S(O<sub>2</sub>)NR<sub>9</sub>-;

$R_8$  is selected from the group consisting of hydrogen, dialkylamino, carboxyl, hydroxyl, alkoxy, sulfonamide, urea, carbamate, diol, alkylsulphonyl, and  $R_{10}$ ;

$R_9$  is H or (C<sub>1</sub>-C<sub>3</sub>)alkyl;

$R_{10}$  is an optionally substituted 5- or 6-membered saturated, unsaturated, or aromatic heterocycle comprising from 1 to 4 heteroatoms; and

$R_{11}$ , is an optionally substituted 5- to 6-membered saturated heterocyclic ring.

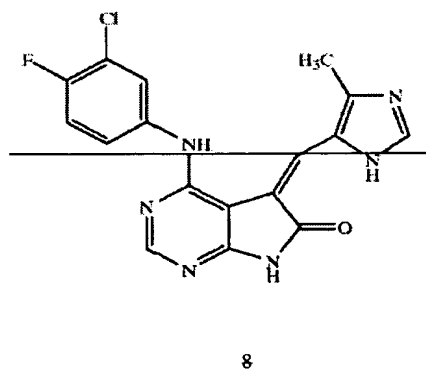
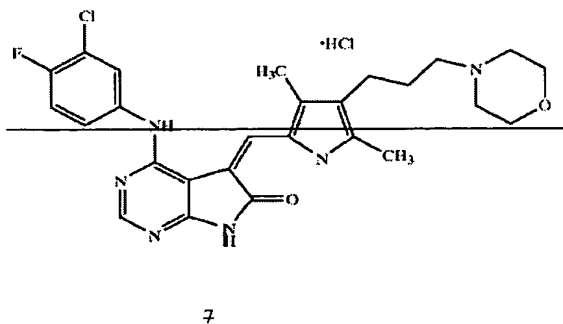
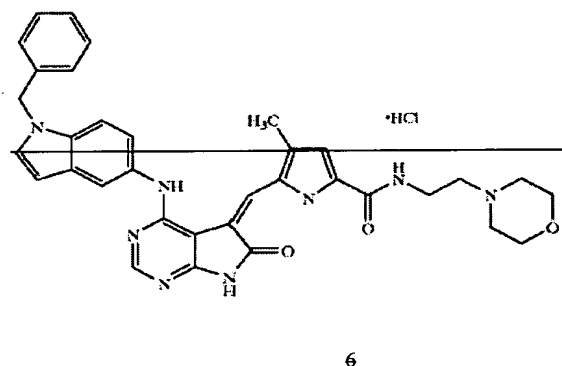
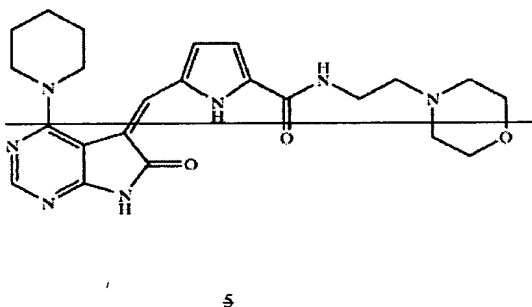
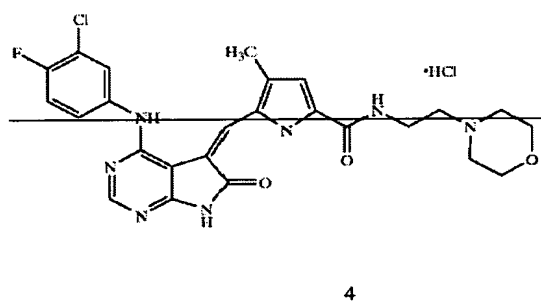
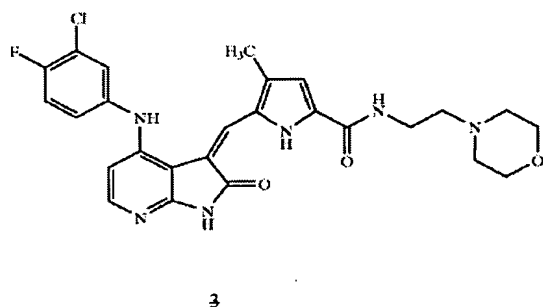
8. (Original) The compound of claim 7 wherein  $R_7$  is  $X_2$ -(C<sub>1</sub>-C<sub>4</sub>)alkyl- $R_8$ ,  $X_2$ -(C<sub>1</sub>-C<sub>4</sub>)alkenyl- $R_8$ , or  $X_2$ -(C<sub>1</sub>-C<sub>4</sub>)alkynyl- $R_8$ , and  $R_8$  is selected from the group consisting

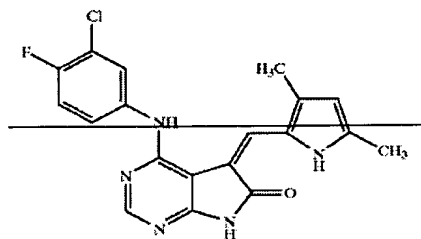
of alkylsulfonyl, alkoxy, carboxyl, morpholino, 1-alkyl-piperazin-4-yl, pyrrolidinyl, piperidinyl, pyridyl, imidazolo, triazolo, tetrazolo, and thiazolo.

9. (Original) The compound of claim 1 wherein  $R_4$  is H, methyl, or trifluoromethyl.

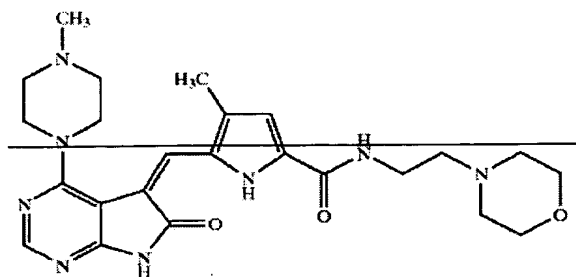
10. (Original) The compound of claim 1 wherein if Z is CH,  $R_1$  is  $CH_3$  or  $R_3$  and  $R_2$  do not form an optionally substituted methylindene.

11. (Currently Amended) A compound selected from the group consisting of:

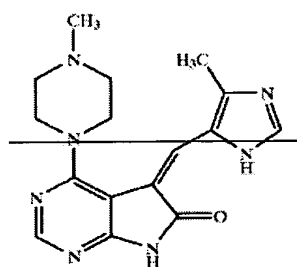




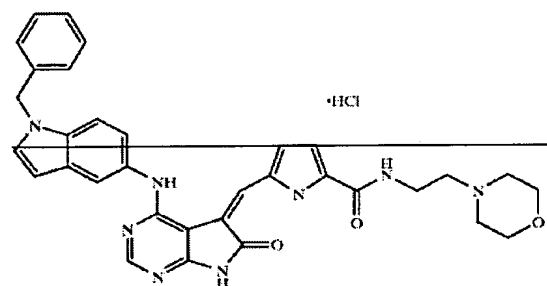
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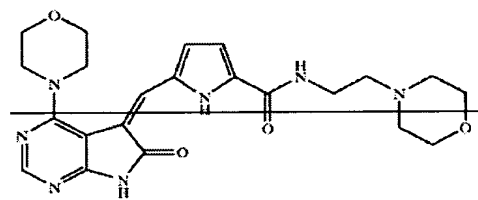
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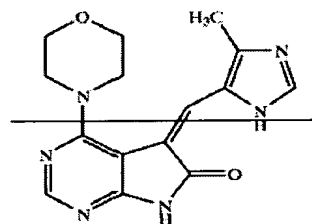
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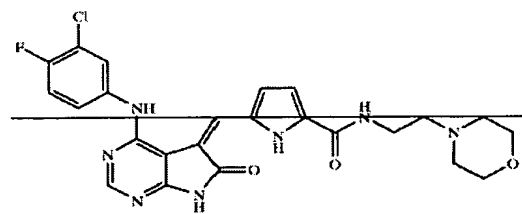
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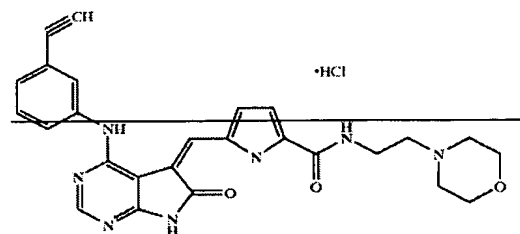
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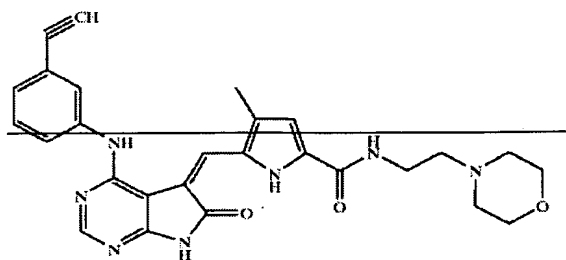
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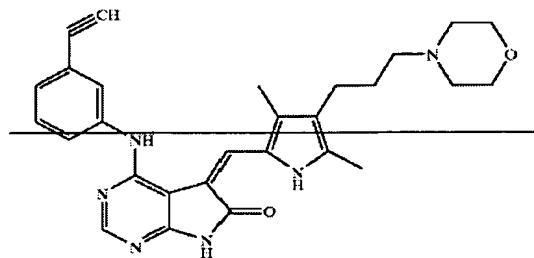
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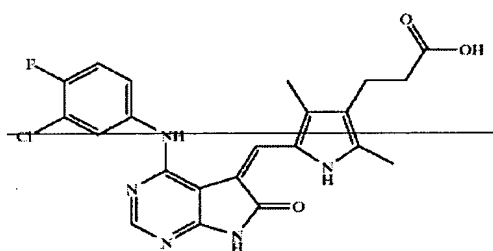
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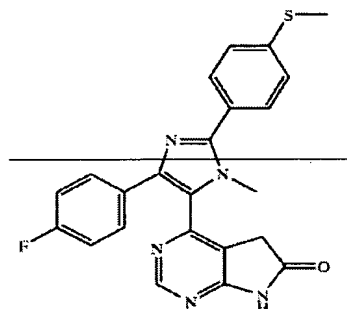
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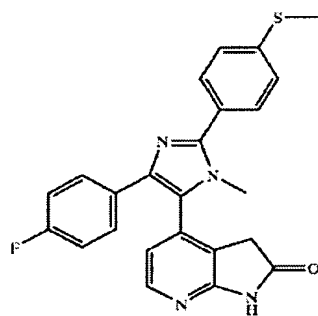
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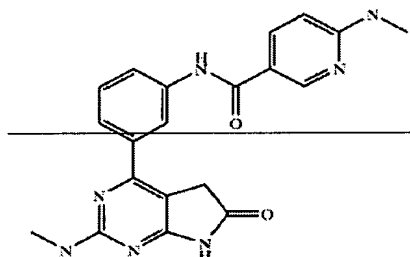
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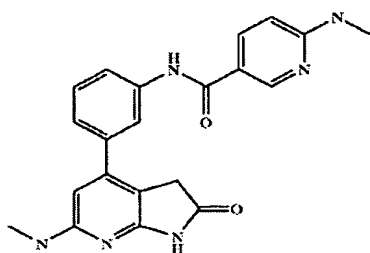
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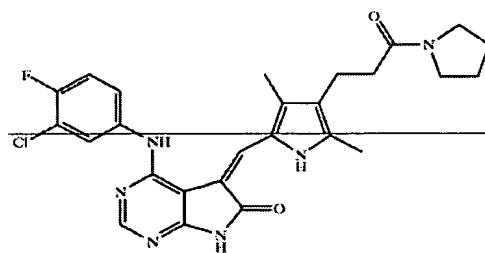
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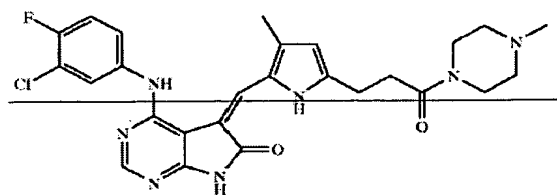
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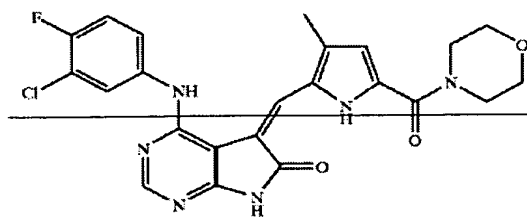
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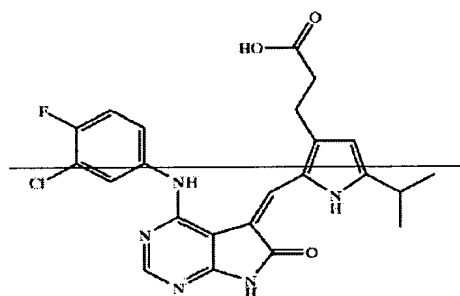
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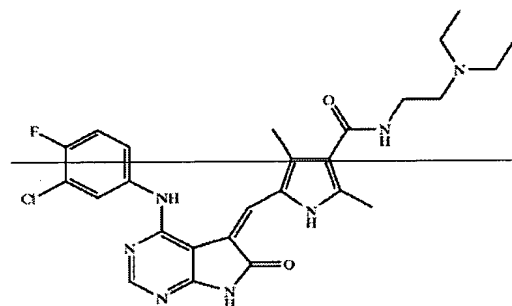
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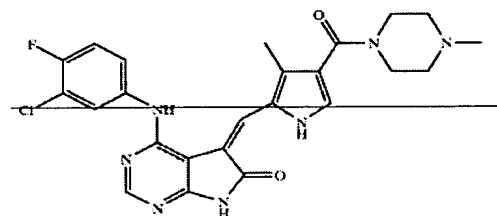
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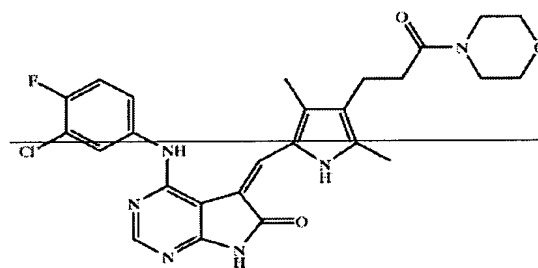
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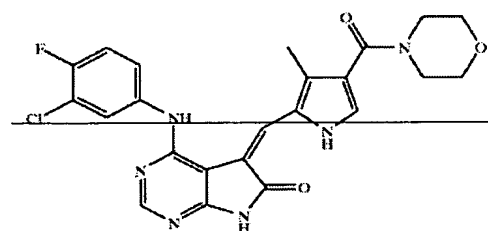
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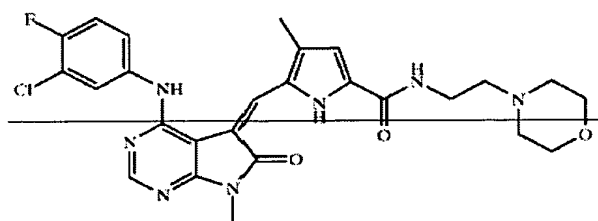
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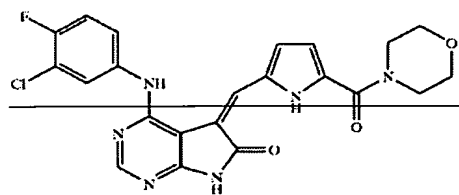
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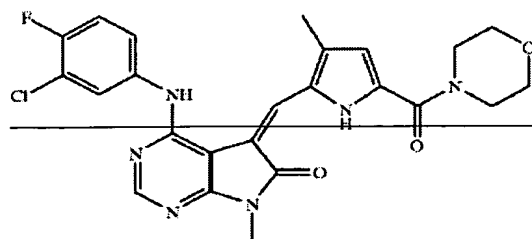
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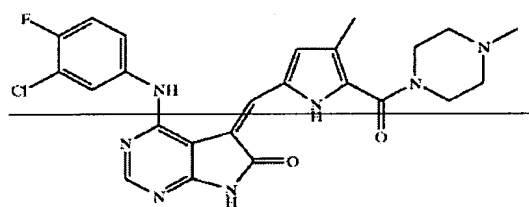
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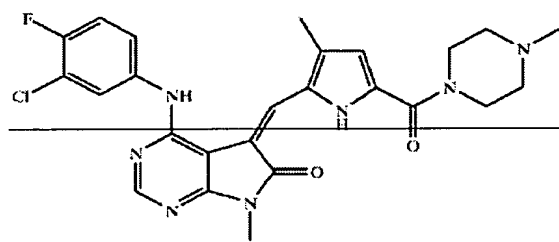
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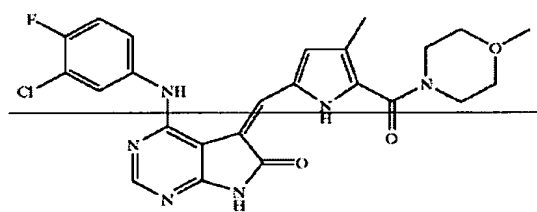
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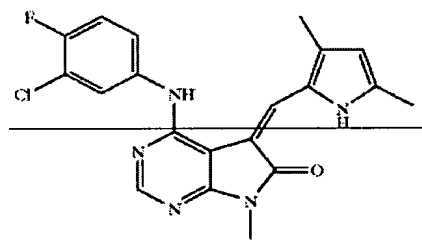
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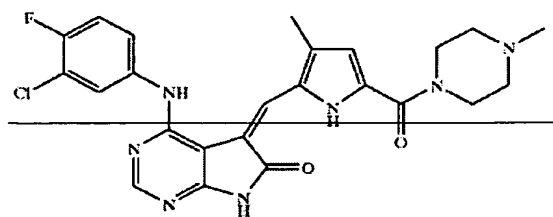
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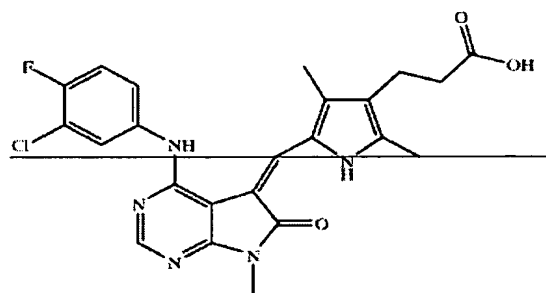
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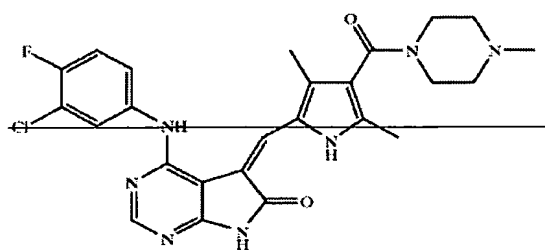


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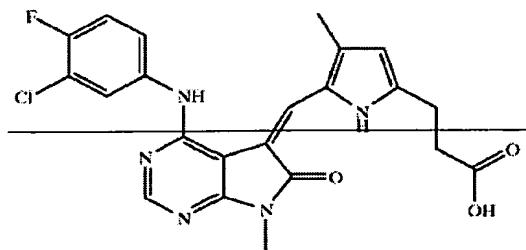


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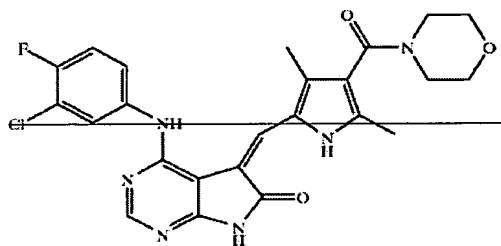




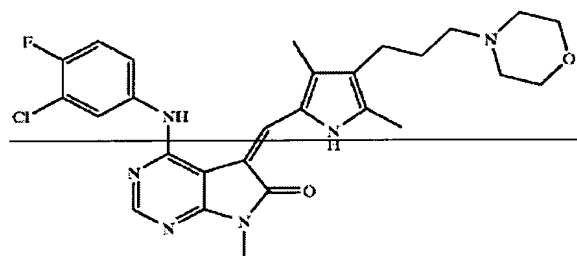
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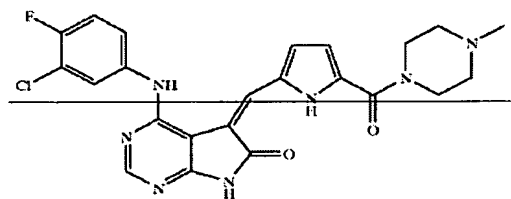
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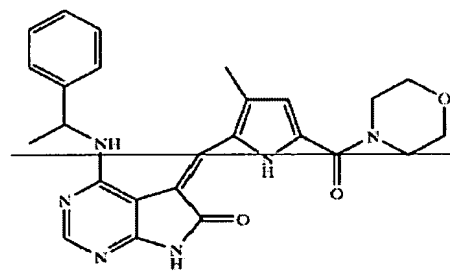
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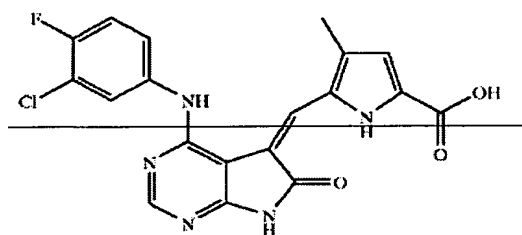
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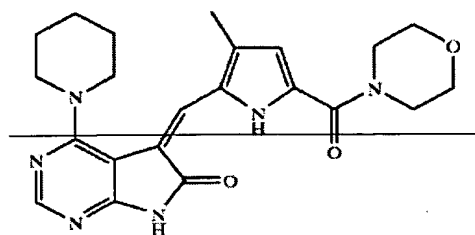
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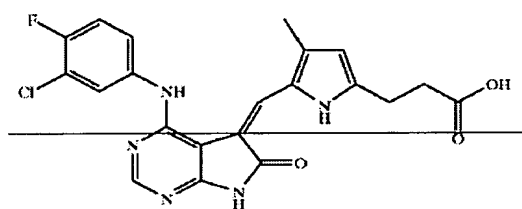
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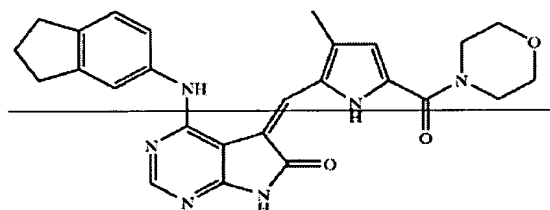
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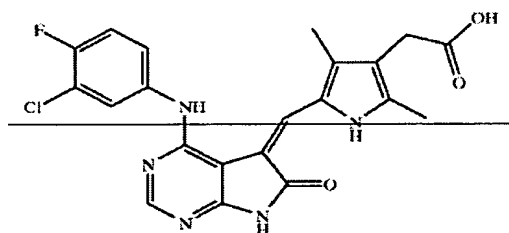
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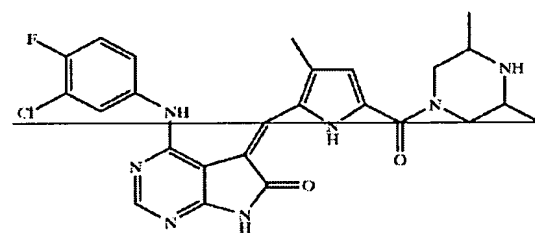
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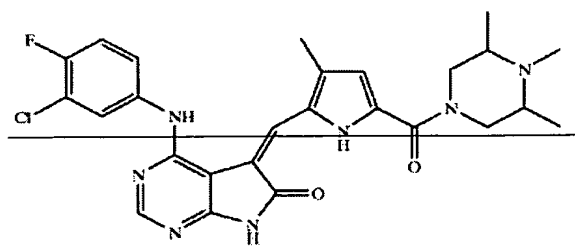
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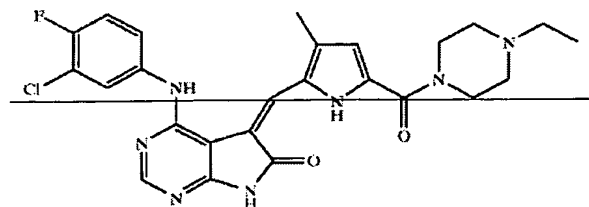
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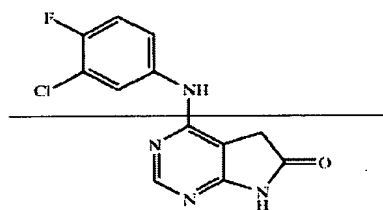
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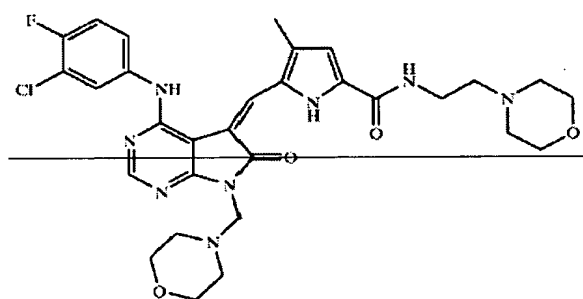
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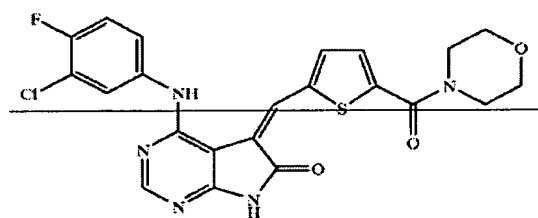
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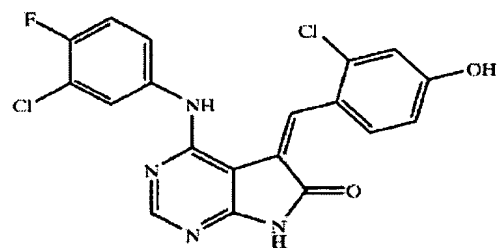
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and pharmaceutically acceptable salts, solvates, clathrates, and prodrugs thereof.

Claims 12 – 21 (Cancelled).

22. (Original) A pharmaceutical composition comprising a compound of Formula 1, or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof, and a pharmaceutically acceptable carrier.

23. (Original) The pharmaceutical composition comprising a compound of claim 11 and a pharmaceutical acceptable carrier or excipient.

24. (Original) The pharmaceutical composition of claim 22 which is suitable for oral, transdermal, topical, parenteral, or mucosal administration.

25. (Original) A method of regulating, modulating, or inhibiting protein kinase activity which comprises contacting a compound of Formula 1, or a pharmaceutically acceptable salt or solvate thereof, with a protein kinase.

26. (Original) The method of claim 25 wherein the protein kinase is a protein tyrosine kinase.

27. (Original) The method of claim 25 wherein the protein kinase is selected from the group consisting of abl, ATK, bcr-abl, Blk, Brk, Btk, c-fms, c-kit, c-met, c-src, CDK1, CDK2, CDK4, CDK6, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, ERK, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, FLK-4, flt-1, Fps, Frk, Fyn, GSK, Gst-Flk1, Hck, Her-2, Her-4, IGF-1R, INS-R, Jak, JNK, KDR, Lck, Lyn, MEK, p38, PANHER, PDGFR, PLK, PKC, PYK2, Raf, Rho, ros, SRC, tie<sub>1</sub>, tie<sub>2</sub>, TRK, UL97, VEGFR, Yes, and Zap70.

28. (Original) The method of claim 27 wherein the protein kinase is selected from the group consisting of PANHER, EGFR, Her-2, Her-4, PDGFR, SRC, Lck, cdk2, p38, Raf, and Rho.

29. (Original) The method of claim 28 wherein the protein kinase is selected from the group consisting of PANHER, CDK2, PDGFR, p38, and Raf.

30. (Original) The method of claim 25 wherein the protein kinase is in a cell culture.

31. (Original) The method of claim 25 wherein the protein kinase is in a mammal.

32. (Original) A method of treating or preventing a mammalian disease characterized by unregulated protein kinase activity which comprises administering to a mammal in need of such treatment or prevention a therapeutically or prophylactically effective amount of a compound of Formula 1, or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

33. (Original) The method of claim 30 wherein the disease characterized by unregulated protein kinase activity is selected from the group consisting of: blood vessel proliferative disorders; fibrotic disorders; mesangial cell proliferative disorders; metabolic disorders; allergies; asthma; thrombosis; nervous system diseases; and cancer.

34. (Original) The method of claim 31 wherein the disease characterized by unregulated protein kinase activity is cancer.

35. (Original) The method of claim 32 wherein the cancer is selected from the group consisting of breast, stomach, ovary, colon, lung, brain, larynx, lymphatic system, genitourinary tract (including bladder and prostate), ovarian, gastric, bone, and pancreatic cancer.